IN THE SPECIFICATION:

Please rewrite the first paragraph on page 4 as follows:

This invention provides an isolated strain of Hepatitis B virus designated Human Hepatitis B Virus Surface Antigen-'S'-145 Singapore Strain (Glycine to Arginine) which constituent viral genome is deposited under Accession Nos. P97121504, P97121505 and P97121506 with the European Collection of Cell Culture on 15th December 1997.

Please rewrite the second paragraph on page 4 as follows:

This invention also provides an isolated nucleic acid encoding a polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus, such polypeptide having an amino acid sequence which differs from the amino acid sequence of a major surface antigen of a wild type hepatitis B virus in that the amino acid at position number 145 of such polypeptide is an arginine rather than a glycine.

Please rewrite the third paragraph on page 4 as follows:

This invention provides a method of producing the polypeptide in purified form and the resulting purified polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus, such polypeptide having an amino acid sequence which differs from the amino acid sequence of a major surface antigen of a wild type hepatitis B virus in that the amino acid at position number 145 of such polypeptide is an arginine rather than a glycine.

Please rewrite the fourth paragraph on page 4 as follows:

This invention provides an oligonucleotide of at least 15 nucleotides capable of specifically hybridizing with sequences of only the mutant viral strain of hepatitis B virus.

Please rewrite the paragraph bridging pages 4 and 5 as follows:

This invention provides a method of obtaining antibodies to a polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus and the antibodies produced. This invention provides a method of determining whether a subject is infected with the above-described viral strain.

Please rewrite the first paragraph on page 11 as follows:

Further, this invention provides a vector comprising an isolated nucleic acid encoding a peptide, wherein the peptide is encoded by a nucleic acid molecule comprising nucleotides 527 through 595 of SEQ. I.D. No. 1.

Please rewrite the second paragraph on page 11 as follows:

In both of the above-identified vectors, the vector may comprise viral DNA.

Please replace the third paragraph on page 11 as follows:

This invention also provides a host vector system for the production of a polypeptide which comprises the above-described vectors in a suitable host.

Please rewrite the fourth paragraph on page 11 as follows:

This invention also provides a method of producing a polypeptide or a peptide which comprises growing the host vector systems described above, under suitable conditions permitting production of the polypeptide and recovering the polypeptide so produced.

Please rewrite the fifth paragraph on page 11 as follows:

This invention further provides a method of obtaining a polypeptide or a peptide in purified form which comprises: (a) introducing the above-described vectors into a suitable host cell; (b) culturing the resulting host cell so as to produce the polypeptide; (c) recovering the polypeptide produced in step (b); and (d) purifying the polypeptide so recovered.

Please rewrite the sixth paragraph on page 11 as follows:

This invention further provides a purified polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus, such polypeptide having an amino acid sequence which differs from the amino acid sequence of a major surface antigen of a wild type hepatitis B virus in that the amino acid at position number 145 of such polypeptide is an arginine rather than a glycine. One means of obtaining the polypeptide is by the above-described method.

Please rewrite the paragraph bridging pages 11 and 12 as follows:

This invention also provides a purified peptide, wherein the peptide has an amino acid sequence comprising amino acid residues 298 through 320 of the amino acid sequence designated Seq. I.D. No. 3. One means of obtaining this peptide is by the above-describe

method.

Please rewrite the paragraph bridging pages 14 and 15 as follows:

Another example is where the nucleic acid sample in step (a) comprises mRNA corresponding to the transcript of DNA encoding a polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus, such polypeptide having an amino acid sequence which differs from the amino acid sequence of a major surface antigen of a wild type hepatitis B virus in that the amino acid at position number 145 of such polypeptide is an arginine, rather than a glycine, and wherein the determining of step (b) comprises: (i) translating the mRNA under suitable conditions to obtain an amino acid sequence; and (ii) comparing the amino acid sequence of step (i) which the amino acid sequence of an isolated nucleic acid which encodes a polypeptide, wherein the polypeptide has an amino acid sequence substantially identical to amino acid residues 174 through 400 of the amino acid sequence designated SEQ.I.D. No. 3 so as to thereby determine whether the nucleic acid sample is, or is derived from, a cucleic acid which encodes the polypeptide. A further example is where the determining of step (b) comprises: (i) amplifying the nucleic acid present in the sample of step (a); and (ii) detecting the presence of polypeptide in the resulting amplified nucleic acid.

Please rewrite the second paragraph on page 15 as follows:

This invention provides the use of an antibody that recognizes a polypeptide which is a mutant major surface antigen of a train of hepatitis B virus for determining whether the subject has a predisposition for hepatocellular carcinoma, wherein such determination comprises: (a)

obtaining an appropriate nucleic acid sample from the subject; and (b) determining whether the nucleic acid sample from step (a) is, or is derived from, a nucleic acid encoding a polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus, such polypeptide having an amino acid sequence which differs from the amino acid sequence of a major surface antigen of a wild type hepatitis B virus in that the amino acid at position number 145 of such polypeptide is an arginine, rather than a glycine, by contacting the sample under appropriate conditions to bind to the antibodies of claim 35 so as to determine whether the subject has a predisposition for hepatocellular carcinoma.

Please rewrite the paragraph bridging pages 15 and 16 as follows:

The invention also provides use of antibodies capable of detecting a polypeptide which is a mutant major surface antigen of a strain of Hepatitis B virus designated Human Hepatitis B Virus Surface Antigen- 'S' -145 Singapore Strain (Glycine to Arginine) for determining whether a subject is infected with a strain of Hepatitis B virus designated Human Hepatitis B Virus Surface Antigen- 'S' -145 Singapore Strain (Glycine to Arginine), wherein such determination comprises: (a) obtaining an appropriate sample from the subject; and (b) determining whether the sample from step (a) is, or is derived from, a nucleic acid encoding a polypeptide which is a mutant major surface antigen of a strain of hepatitis B virus, such polypeptide having an amino acid sequence which differs from the amino acid sequence of a major surface antigen of a wild type hepatitis B virus in that the amino acid at position number 145 of such polypeptide is an arginine, rather than a glycine by contacting the sample under appropriate conditions to bind to the antibodies so as to determine whether a subject is infected. Furthermore, the antibody may

also be capable detecting a peptide, wherein the peptide has an amino acid sequence comprising amino acid residues 298-320 of the amino acid sequence designated SEQ. I..D. No. 3.

Please rewrite the first paragraph on page 18 as follows:

The actual effective amount will be based upon the size of the polypeptide, the biodegradability of the polypeptide, the bioactivity of the polypeptide and the bioavailability of the polypeptide. If the polypeptide does not degrade quickly, is bioavailable and highly active, a smaller amount will be required to be effective. The effective amount will be known to one of skill in the art; it will also be dependent upon the form of the polypeptide, the size of the polypeptide and the bioactivity of the polypeptide. Use of an adjuvant for example, would lower the required amount of the polypeptide. One of skill in the art could routinely perform empirical activity tests to determine the bioactivity in bioassays and thus determine the effective amount.

Please rewrite the second paragraph on page 18 as follows:

Pharmaceutically acceptable carriers are well known to those skilled in the art and include, but are not limited to, 0.01-0.1M and preferably 0.05M phosphate buffer or 0.8% saline. Additionally, such pharmaceutically acceptable carriers may be aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions,

including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers such as those based on Ringer's dextrose, and the like. Preservatives and other additives may also be present, such as, for example, antimicrobials, antioxidants, chelating agents, inert gases and the like.

Please rewrite the paragraph bridging pages 18 and 19 as follows:

This invention further provides a composition comprising a peptide, wherein the peptide has an amino acid sequence comprising amino acid residues 298 through 320 of the amino acid sequence designated SEQ. I.D. No. 3 or derivative thereof, the amounts of such peptide being effective to stimulate or enhance antibody production in a subject, and a pharmaceutically acceptable carrier.

Please rewrite the first paragraph on page 32 as follows:

In addition, these features allow accurate diagnosis of patients at an early stage of the disease and also help to remove with higher efficiency blood contaminated with vaccine-induced mutant hepatitis B virus through using a screening test of donor bloods.

Please rewrite the second paragraph on page 32 as follows:

Proteins and their antibodies under the present invention can be utilized for development of prophylactic and therapeutic vaccines, as well as, immunological pharmaceuticals. Sequence information on structural genes of these mutant viruses will be helpful in developing detection

systems of the relevant protein antigens and antibodies.

Please rewrite the third paragraph on page 32 as follows:

Antigen-antibody complexes can be detected by known methods. Specific monoclonal and polyclonal antibodies can be raised by immunizing animals such as mice and rabbits with peptides or proteins specific to mutant vaccine-induced hepatitis B viruses. Inhibitory antiviral agents can be designed and targeted against these proteins and molecules in cell culture or in vivo.

Please rewrite the fourth paragraph on page 32 as follows:

The present invention is based on studies on an isolated virus genome with a vaccine-induced mutation at amino acid residue 145 (Glycine to Arginine) of the major surface antigen. The invention makes possible highly specific detection of these vaccine-induced mutant hepatitis B virus and provides materials such as protein, polyclonal and monoclonal antibodies for development of such detection system.

Please rewrite the paragraph bridging pages 32 and 33 follows:

We have evidence showing that when expressed in a mammalian expression system, the major surface antigen (HBsAg) of the mutant HBV reported in our invention is detected as a 22kDa protein on a Coomassie-blue stained SDS-PAGE gel, whereas the wild type HBsAg is detected as a 25kDa protein. Since the only glycosylation site on the HBsAg is located in close proximity (Asparagine at position 146) to the mutation at position 145, it is very likely that the

drastic change from Glycine to Arginine at position 145 affects the glycosylation process in the mutant HBsAg. This defective glycosylation process would in turn result in the smaller protein as observed in our studies. As the antigenicity of a protein is adversely affected by the extent of its glycosylation, we predict that the mutant HBsAg reported in our invention is more antigenic than the wild type HBsAg. This prediction is further supported by the structural analysis using the method developed by Hopp and Woods.

Please delete the sequence listing and substitute the sequence listing attached hereto.